REMARKS

Claims 1-5 are pending in the application. No new matter has been inserted into the application. The amendments to the claims have been made merely to further clarify the presently claimed invention. Accordingly, entry of the amendments to the application is respectfully requested.

Rejection Under 35 U.S.C. 112, first paragraph – New Matter

Claims 1-5 and 13-15 have been rejected under 35 U.S.C. 112, first paragraph because the application allegedly contains new matter regarding the production of connective tissue. The claims have been amended so that hyaline cartilage is regenerated. Accordingly, this rejection has been overcome.

Rejection Under 35 U.S.C. 112, first paragraph

Claims 1-5 and 13-15 have been rejected under 35 U.S.C. 112, first paragraph because the specification allegedly does not provide an enabling disclosure for the claimed invention.

The presently claimed invention is directed to a method of treating osteoarthritis, which includes:

a) generating a recombinant viral or plasmid vector comprising a DNA sequence encoding transforming growth factor β1 or BMP-2 operatively linked to a promoter;

b) transfecting *in vitro* a population of chondrocytes with said recombinant vector, resulting in a population of transfected chondrocytes; and

c) transplanting said transfected chondrocytes without scaffolding by intraarticular injection to an osteoarthritic joint space of a mammalian host, such that expression of said DNA sequence within said joint space results in regenerating hyaline cartilage.

In the presently claimed invention, chondrocytes are transfected or transduced with TGFβ1 or BMP-2 and the resultant composition along with a pharmaceutical carrier which does not include scaffolding or any other such physical matrix is injected into the joint space to regenerate hyaline cartilage. Using chondrocytes is disclosed at least at pages 5 and 9 in the present application. Use of BMP-2 protein is discussed at least at page 5 in the present specification.

To further indicate support for "treating osteoarthritis with chodrocyte transfected with TGF-β1 or BMP-2", the Examiner's attention is directed to page 1 in the specification of the present application where the following passage is found:

"In the orthopedic field, degenerative arthritis or osteoarthritis is the most frequently encountered disease associated with cartilage damage. Almost every joint in the body, such as the knee, the hip, the shoulder, and even the wrist, is affected. The pathogenesis of this disease is the degeneration of hyaline articular cartilage (Mankin et al., J Bone Joint Surg, 52A: 460-466, 1982). The hyaline cartilage of the joint becomes deformed, fibrillated, and eventually excavated. If the degenerated cartilage could somehow be regenerated, most patients would be able to enjoy their lives without debilitating pain."

Since the present application discloses that hyaline cartilage is made using chondrocytes transfected with TGF-β1 or BMP-2, it is within the purview of the present invention that osteoarthritis is also treated by injecting to a patient suffering from osteoarthritis a substance that generates hyaline cartilage, which include chondrocytes bearing TGF-β1 or BMP-2.

Applicants respectfully submit that given the guidance presented in the instant specification, a person of ordinary skill in the art would know how to transfect or transduce chondrocyte with genes encoding TGFβ1 or BMP-2 and inject them into the knee joint. These are discussed in detail in which fibroblast/TGFβ1 has been specifically and without

limitation exemplified. However, the application explicitly allows for the use of chondrocytes to regenerate cartilage following the same or similar method as using fibroblasts applying well-known molecular biological techniques. Thus, applicants submit that the present application provides a fully enabling description of the presently claimed invention.

Applicants respectfully submit that given the guidance presented in the instant specification, the application provides an enabling disclosure for treating osteoarthritis especially considering the regeneration of hyaline cartilage in rabbits as exemplified in the present application. Regeneration of hyaline cartilage can be thought of as *de facto* treating osteoarthritis because osteoarthritis is caused by the mechanical wearing away of the cartilage, and thus regeneration of cartilage replenishes the degraded cartilage to treat osteoarthritis. Furthermore, no immuno-rejection is seen by the inventive procedure. Thus, applicants submit that the present application provides a fully enabling description of the presently claimed invention. Withdrawal of this rejection is respectfully requested.

The Examiner continues to assert that there is a lack of equivalence between TGFβ1 and BMP-2. However, Applicants submit that both of these proteins belong to the TGFβ1 superfamily. As a result, the activity of one protein is reasonably expected to provide the same type of activity unless there is reason to assume why BMP-2 would not work in the osteoarthritic treatment protocol. Applicants assert that the Examiner has failed to meet this burden of initially providing any reason why the BMP-2 gene would not be effective is hyaline cartilage generation and further, if there would be any undue experimentation to determine its effects on cartilage regeneration and by extension to osteoarthritis.

The Examiner also contends that fibroblasts are not equivalent to chondrocytes. In response, Applicants submit that methods of inserting a gene into a chondrocyte is a well-known process. Further, in the present application, Applicants have exemplified fibroblasts as cells that can generate cartilage. However, this does not mean that Applicants should be

limited to use of fibroblasts only. Connective tissue cells may be used. In particular, chondrocytes have been pointed as being especially useful to the practice of the presently claimed invention. Therefore, Applicants respectfully request the Examiner to withdraw this rejection.

Examiner has also asserted that the animal data presented in the present application are not persuasive of treatment of osteoarthritis. In response, Applicants note that data using the rabbit model such as presented in the present application was used for submission of an Investigational New Drug application to the FDA for treatment of degenerative arthritis. Osteoarthritis is considered to be a degenerative arthritis. The FDA granted the application, based in part on the data gathered using the rabbit model and also data from goat. Therefore, it is believed that the results obtained using the rabbit animal models as presented in the present application provides data sufficient to be predictive of efficacy in degenerative arthritis such as osteoarthritis.

Rejection Under 35 U.S.C. 112, second paragraph

Claims 1-5 and 13-15 have been rejected as being indefinite. The claims have been amended in order to remove the objected to language. Thus, this rejection has been overcome.

Obviousness-Type Double Patenting

Claims 1-5 and 13-15 have been provisionally rejected under the judicially created doctrine of obviousness type double patenting over claims 1-11 of U.S. Patent No. 6,797,703, application number 09/702,718. Applicants traverse this rejection. Reconsideration and withdrawal of this rejection are respectfully requested. Applicants will consider filing a terminal disclaimer when the application is in otherwise allowable condition.

Claims are free of prior art

Applicants note the Examiner's indication that the claims are free of prior art.

Conclusion

It is believed that the application is now in condition for allowance. Applicants request the Examiner to issue a notice of Allowance in due course. The Examiner is encouraged to contact the undersigned to further the prosecution of the present invention.

The Commissioner is authorized to charge JHK Law's Deposit Account No. **502486** for any fees required under 37 CFR §§ 1.16 and 1.17 that are not covered, in whole or in part, by a credit card payment enclosed herewith and to credit any overpayment to said Deposit Account No. **502486**.

Respectfully submitted,

JHK Law

Dated: December 8, 2006

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